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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/376,604	08/18/99	MADIYALAKAN R	107823.129

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EXAMINER	
TRAN, M	
ART UNIT	PAPER NUMBER
1642	14

DATE MAILED:
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/376,604	MADIYALAKAN ET AL.	
	Examiner	Art Unit	
	MAU T TRAN	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *113,115-135,137-144 and 170-209* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *113,115-135,137-144 and 170-209* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,13* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

This application is a CIP of PCT IB96/00461 filed May 15, 1996 which is a CIP of US Application 08/877302 filed June 1997 which is a CIP of Us Application No. 09/094598 filed June 15, 1998 (now abandoned) which is a CIP of US Application 09/152698 filed September 2, 1998 which is a CIP of PCT IB99/01114 filed June 15, 1999. A preliminary amendment was received on April 20, 2001 in which claims 114, 136 and 145-169 were cancelled without prejudice and claims 115-118, 122, 126, 129, 131, 132, 134, 137, 138 and 140-142 were amended and new claims 170-209 were added. Claims 113, 115-135, 137-144, 170-209 are pending.

REMARK: On the file receipt, this application also claims to be a CIP of 09/376604 which is the instant application. It is requested that Applicant clarifies this claim for priority.

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 113, 115-135 and 137-144 in Paper No. 12 is acknowledged. New claims 170-173 depend from original claim 135. Claims 113, 115-135, 137-144 and 170-209 are examined on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to and claims 113, 115-135, 137-144 and 170-209 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from a written description (e.g. sequenced); or (3) deposited.

It unclear if a cell line which produces an antibody having the exact structural and chemical identity of B43.13 antibody is known and publicly available, or can be

reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

The instant application does not provide the appropriate evidence of satisfying the deposit of the cell line producing B43.13 antibody for the enforceable life of the patent.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications. Applicant's provision of these assurances would obviate this objection/rejection.

Affidavits and declarations, such as those under 37 C.F.R. § 1.131 and 37 C.F.R. § 1.132, filed during prosecution of the parent application do not automatically become a part of this application. Where it is desired to rely on an earlier filed affidavit, the applicant should make the remarks of record in the later application and include a copy of the original affidavit filed in the parent application.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 113, 115-126, 128-132, 135, 137-140, 174-188, 190-194, 196, 201-205 are rejected under 35 U.S.C. 102(b) as being anticipated by Madiyalakan et al (Hybridoma, April 1995, Vol. 14(2):199-203.

Claims 113, 115-126, 128-132, 135, 137-140, 174-188, 190-194, 196, 201-205 are drawn to a method of inducing a therapeutic host immune response against a multi-epitopic soluble in vivo antigen that does not elicit an effective host immune response by contacting the antigen with a binding agent that binds to the antigen to form the agent/antigen pair whereby an effective host immune response is elicited against a second epitope on the antigen in the agent/antigen pair such that the agent is the antibody B43.13 and the antigen is CA125 wherein the antibody is radiated and given at a dose of .1 microgram to 2 milligram/kg of body weight and the serum level of CA125 is greater than 100 U/ml in the host serum and the antibody/antigen complex does not induce an HAMA toxicity.

Madiyalakan et al taught a method using the radiated chimeric monoclonal antibody B43.13 which is soluble and its anti-idiotypes (Ab2 and Ab3) against the CA125 antigen which is an in vivo antigen found on cancerous cells at a dose of 2 mg/kg of body weight wherein the serum levels for the CA125 is greater than 100 U/ml (See Table 1 and Figure 1) and does not induce an HAMA toxicity and the antibody is given in sufficient amount to present the antigen to the immune system as recorded by the production of anti-idiotype antibodies and given through an immunological route (evidenced by the serum titers of the antibody). The antibody administration was found to induce both an immune response (cellular and humoral).

REMARK: The scope of the claims read on antibody/antigen induction of an immune response but does not specifically suggests the claiming of anti-idiotype antibodies though that is what is disclosed in the specification.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a). See also REMARK after 102(b) rejection.

Claims 113, 115-135, 137-144, 170-209 are rejected under 35 U.S.C. 103(a) as being unpatentable over Madiyalakan et al (Hybridoma, April 1995, Vol. 14(2):199-203 in view of Baum et al (Hybridoma, 1993, Vol. 12(5):583-9) or Baum et al (Cancer Supplement, 1994, Vol. 73(3):1121-1125).

Claims 113, 115-135, 137-144, 170-209 are drawn to a method of inducing a therapeutic host immune response against a multi-epitopic in vivo soluble antigen that does not elicit an effective host immune response by contacting the antigen with a binding agent that binds to the antigen to form the agent/antigen pair whereby an effective host immune response is elicited against a second epitope on the antigen in the agent/antigen pair such that the agent is the antibody B43.13 and the antigen is CA125 wherein the antibody is radiated and given at a dose of .1 microgram to 2 milligram/kg of body weight and the serum level of CA125 is greater than 100 U/ml in the host serum and the antibody/antigen complex does not induce an HAMA toxicity.

Madiyalakan et al taught a method using the radiated chimeric monoclonal antibody B43.13 which is soluble and its anti-idiotypes (Ab2 and Ab3) against the CA125 antigen which is an in vivo antigen found on cancerous cells at a dose of 2 mg/kg of body weight wherein the serum levels for the CA125 is greater than 100 U/ml (See Table 1 and Figure 1) and does not induce an HAMA toxicity and the antibody is given in sufficient amount to present the antigen to the immune system as recorded by the production of anti-idiotype antibodies and given through an immunological route (evidenced by the serum titers of the antibody). The antibody administration was found to induce both an immune response (cellular and humoral) but differ from the instant invention by not disclosing an adjuvant with the antibody.

Baum et al teaches the use of radiolabeled monoclonal antibody B43.13 which is specific for the CA125 antigen in ovarian cancer but does not disclose using anti-idiotypic antibodies (B2 or B3).

Baum et al teaches the use of B43.13 antibody against the CA125 antigen and suggests that the anti-idiotype antibody (B3) would be beneficial in suppression of ovarian cancer growth in patients.

Therefore, it would have been *prima facie* obvious for one of the ordinary skill in the art, at the time the invention, was made to combine the teachings of Madiyalakan et al with that of either Baum et al (Hybridoma reference) or Baum et al (Cancer Supplement reference) to derive at a method of inducing an immune response by using an antibody of B43.13 against the CA125 antigen to induce an immune response that would suppress cancer growth. It was already known at the time as evidenced by these references that an antibody that is specific for CA125 was already in use and known to induce an anti-idiotype antibody response as a result of the B43.13 antibody administration helped to suppress the cancer growth.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 113, 115-135, 137-144, 170-209 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,241,985. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the US Patent '985 do not claim the dose limitation of the CA125 serum level of greater than 100 U/ml and the dose of the antibody at .1-2 mg/kg body weight. However the claims in both the instant application and the patent are drawn to a method of inducing an immune response (induction of antibodies) to a multi-epitopic endogenous antigen wherein the antigen is CA125 and the antibody is B43.13.

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mau Tran whose telephone number is 703-605-1165. The examiner can normally be reached on Monday-Friday from 8:00 a.m. – 5:30 p.m. with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. Any inquiry of a general

nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Mau Tran, Ph.D.
Patent Examiner, Art Unit 1642
June 13, 2001

GEETHA P. BANSAL
PRIMARY EXAMINER